

### AMENDMENTS TO THE CLAIMS

1. (CURRENTLY AMENDED) A method for treating neuropathic pain without alleviating acute pain, comprising:

identifying a subject in need of such treatment; and

providing the subject with an effective amount of at least one compound that selectively activates the M(1) receptor subtype, whereby one or more symptoms of the neuropathic pain are reduced and wherein the compound does not alleviate acute pain.

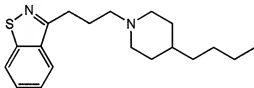
2. (ORIGINAL) The method of claim 1, wherein the subject presents hyperalgesia.

3. (ORIGINAL) The method of claim 1, wherein the subject presents allodynia.

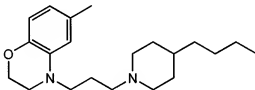
4. (ORIGINAL) The method of claim 1, wherein the neuropathic pain is associated with diabetes, viral infection, irritable bowel syndrome, amputation, cancer, or chemical injury.

5. (CANCELED)

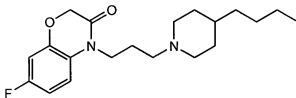
6. (ORIGINAL) The method of claim 1, wherein the compound is selected from the group consisting of the compounds of Formulas VII, VIII, and IX:



(VII)



(VIII)



(IX)

7. (CURRENTLY AMENDED) A method of identifying a compound that alleviates hyperalgesia or allodynia in a subject without alleviating acute pain, comprising:

providing the subject with at least one selective muscarinic receptor test compound; and

determining if the at least one test compound reduces hyperalgesia or allodynia in the subject without alleviating acute pain.

8. (ORIGINAL) The method of claim 7, wherein the at least one test compound is selective for the M(1) or M(4) but not M(2) or M(3) receptor.

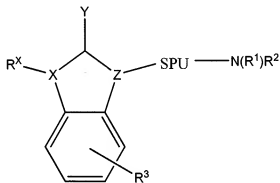
9. (ORIGINAL) The method of claim 7, wherein the at least one test compound is selective for the M(1) receptor.

10. (ORIGINAL) The method of claim 7, wherein the hyperalgesia is thermal hyperalgesia.

11. (ORIGINAL) The method of claim 7, wherein the allodynia is tactile allodynia.

12-13. (CANCELED)

14. (NEW) The method of claim 1, wherein the compound has the structure of formula (I):



(I)

wherein

X is selected from the group consisting of C, O, N and S;

Z is selected from the group consisting of CH and N;

Y is selected from the group consisting of =O, =N and =S or tautomers thereof, such as Y-alkylated tautomers;

SPU is a spacer unit providing a distance d between Z and N wherein —SPU— is a biradical selected from the group consisting of —(CR<sup>6</sup>R<sup>7</sup>)<sub>n</sub>—A— and —

C<sub>3-8</sub>-cycloalkyl-, wherein n is in the range 1 to 5, such as 1, 2, 3, 4, or 5 and A is absent or an optionally substituted —C<sub>3-8</sub>-cycloalkyl;

N together with R<sup>1</sup> and R<sup>2</sup> form a heterocyclic ring wherein said heterocyclic ring is selected from the group consisting of perhydroazocine, perhydroazepine, piperidine, pyrrolidine, azetidine, aziridine and 8-azabicyclo[3.2.1]octane and wherein the heterocyclic ring is substituted with one or more substituents R<sup>4</sup> selected from the group consisting of hydroxy, halogen, C<sub>1-8</sub>-alkyl, C<sub>3-8</sub>-cycloalkyl, C<sub>1-8</sub>-alkoxy, C<sub>1-8</sub>-alkylcarbonyl, C<sub>1-8</sub>-alkylidene, C<sub>2-8</sub>-alkenyl, C<sub>2-8</sub>-alkynyl, C<sub>1-6</sub>-alkyloxyimino, and C<sub>1-6</sub>-alkyloxyamino each of which may be optionally substituted with a substituent R<sup>5</sup> and wherein at least one of said substituents R<sup>4</sup> is R<sup>4'</sup> selected from the group consisting of C<sub>1-8</sub>-alkyl, C<sub>3-8</sub>-cycloalkyl, C<sub>1-8</sub>-alkoxy, C<sub>1-8</sub>-alkylcarbonyl, C<sub>1-8</sub>-alkylidenec, C<sub>1-8</sub>-alkyloxyimino, and C<sub>1-8</sub>-alkyloxyamino each of which may be optionally substituted with a substituent R<sup>5</sup>;

R<sup>5</sup> is selected from the group consisting of hydrogen, halogen, hydroxy, C<sub>1-8</sub>-alkyl, C<sub>1-8</sub>-alkoxy, C<sub>3-8</sub>-cycloalkyl, C<sub>3-8</sub>-heterocyclyl, C<sub>1-8</sub>-alkylcarbonyl, C<sub>1-8</sub>-alkylidene, C<sub>2-8</sub>-alkenyl and C<sub>2-8</sub>-alkynyl;

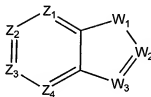
R<sup>X</sup> may be absent or selected from the group consisting of hydrogen, optionally substituted C<sub>1-8</sub>-alkyl, optionally substituted C<sub>3-8</sub>-cycloalkyl, optionally substituted C<sub>2-8</sub>-alkenyl, optionally substituted C<sub>2-8</sub>-alkynyl, optionally substituted aryl, optionally substituted heteroaryl CH<sub>2</sub>—N(R<sup>5</sup>)(R<sup>5</sup>), CH<sub>2</sub>—OR<sup>5</sup>, CH<sub>2</sub>—SR<sup>5</sup>, CH<sub>2</sub>—O—C(=O)R<sup>5</sup>, CH<sub>2</sub>—O—C(=S)R<sup>5</sup>;

R<sup>3</sup> may be present 0-4 times and selected from the group consisting of halogen, hydroxy, optionally substituted C<sub>1-8</sub>-alkyl, C<sub>1-8</sub>-alkoxy, optionally substituted C<sub>1-8</sub>-alkylidene, optionally substituted C<sub>2-8</sub>-alkenyl, optionally substituted C<sub>2-8</sub>-alkynyl optionally substituted aryl, optionally substituted heteroaryl, optionally substituted C<sub>3-8</sub>-cycloalkyl, optionally substituted C<sub>3-8</sub>-heterocyclyl, and optionally substituted C<sub>1-8</sub>-alkylcarbonyl; and

each R<sup>6</sup> and each R<sup>7</sup> is independently selected from the group consisting of hydrogen, halogen, hydroxy, optionally substituted C<sub>1-8</sub>-alkyl, C<sub>1-8</sub>-alkoxy, optionally substituted C<sub>1-8</sub>-alkylidene, optionally substituted C<sub>2-8</sub>-alkenyl, optionally substituted C<sub>2</sub>-

8-alkynyl optionally substituted aryl, optionally substituted heteroaryl, optionally substituted C<sub>3-8</sub>-cycloalkyl, optionally substituted C<sub>3-8</sub>-heterocyclyl, and optionally substituted C<sub>1-8</sub>-alkylcarbonyl.

15. (NEW) The method of claim 1, wherein the compound has the structure of formula (II):



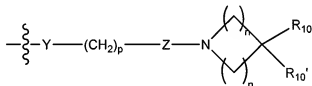
(II)

wherein:

Z<sub>1</sub> is CR<sub>1</sub> or N, Z<sub>2</sub> is CR<sub>2</sub> or N, Z<sub>3</sub> is CR<sub>3</sub> or N, and Z<sub>4</sub> is CR<sub>4</sub> or N, where no more than two of Z<sub>1</sub>, Z<sub>2</sub>, Z<sub>3</sub> and Z<sub>4</sub> are N;

W<sub>1</sub> is O, S, or NR<sub>5</sub>, one of W<sub>2</sub> and W<sub>3</sub> is N or CR<sub>6</sub>, and the other of W<sub>2</sub> and W<sub>3</sub> is CG; W<sub>1</sub> is NG, W<sub>2</sub> is CR<sub>5</sub> or N, and W<sub>3</sub> is CR<sub>6</sub> or N; or W<sub>1</sub> and W<sub>3</sub> are N, and W<sub>2</sub> is NG;

G is of formula (III):



(III)

Y is O, S, CHOH, —NHC(O)—, —C(O)NH—, —C(O)—, —OC(O)—, —(O)CO—, —NR<sub>7</sub>—, —CH=N—, or absent;

p is 1, 2, 3, 4 or 5;

Z is CR<sub>8</sub>R<sub>9</sub> or absent;

each t is 1, 2, or 3;

each R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, and R<sub>4</sub>, independently, is H, amino, hydroxyl, halo, or straight- or branched-chain C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> heteroalkyl, C<sub>1-6</sub> haloalkyl, —CN, —CF<sub>3</sub>—OR<sub>11</sub>, —COR<sub>11</sub>, —NO<sub>2</sub>, —SR<sub>11</sub>, —NHC(O)R<sub>1</sub>, —C(O)NR<sub>12</sub>R<sub>13</sub>, —NR<sub>12</sub>R<sub>3</sub>, —NR<sub>11</sub>C(O)NR<sub>12</sub>R<sub>13</sub>, —SO<sub>2</sub>NR<sub>12</sub>R<sub>13</sub>, —OC(O)R<sub>11</sub>, —O(CH<sub>2</sub>)<sub>4</sub>NR<sub>12</sub>R<sub>13</sub>, or —

$(CH_2)_qNR_{12}R_{13}$ , where  $q$  is an integer from 2 to 6, or  $R_1$  and  $R_2$  together form  $-NH-N=N-$  or  $R_3$  and  $R_4$  together form  $-NH-N=N-$ ;

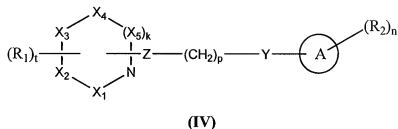
each  $R_5$ ,  $R_6$ , and  $R_7$ , independently, is H,  $C_{1-6}$  alkyl; formyl;  $C_{3-6}$  cycloalkyl;  $C_{5-6}$  aryl, optionally substituted with halo or  $C_{1-6}$  alkyl; or  $C_{5-6}$  heteroaryl, optionally substituted with halo or  $C_{1-6}$  alkyl; each  $R_8$  and  $R_9$ , independently, is H or straight- or branched-chain  $C_{1-8}$  alkyl;

$R_{10}$  is straight- or branched-chain  $C_{1-8}$  alkyl,  $C_{2-8}$  alkenyl,  $C_{2-8}$  alkynyl,  $C_{1-8}$  alkylidene,  $C_{1-8}$  alkoxy,  $C_{1-8}$  heteroalkyl,  $C_{1-8}$  aminoalkyl,  $C_{1-8}$  haloalkyl,  $C_{1-8}$  alkoxycarbonyl,  $C_{1-8}$  hydroxyalkoxy,  $C_{1-8}$  hydroxyalkyl,  $-SH$ ,  $C_{1-8}$  alkylthio,  $-O-CH_2-C_{5-6}$  aryl,  $-C(O)-C_{5-6}$  aryl substituted with  $C_{1-3}$  alkyl or halo,  $C_{5-6}$  aryl,  $C_{5-6}$  cycloalkyl,  $C_{5-6}$  heteroaryl,  $C_{5-6}$  heterocycloalkyl,  $-NR_{12}R_{13}$ ,  $-C(O)NR_{12}R_{13}$ ,  $-NR_{11}C(O)NR_{12}R_{13}$ ,  $-CR_{11}R_{12}R_{13}$ ,  $-OC(O)R_{11}$ ,  $-(O)(CH_2)_sNR_{12}R_{13}$  or  $-(CH_2)_sNR_{12}R_{13}$ ,  $s$  being an integer from 2 to 8;

$R_{10}'$  is H, straight- or branched-chain  $C_{1-8}$  alkyl,  $C_{2-8}$  alkenyl,  $C_{2-8}$  alkynyl,  $C_{1-8}$  alkylidene,  $C_{1-8}$  alkoxy,  $C_{1-8}$  heteroalkyl,  $C_{1-8}$  aminoalkyl,  $C_{1-8}$  haloalkyl,  $C_{1-8}$  alkoxycarbonyl,  $C_{1-8}$  hydroxyalkoxy,  $C_{1-8}$  hydroxyalkyl, or  $C_{1-8}$  alkylthio; each  $R_{11}$ , independently, is H, straight- or branched-chain  $C_{1-8}$  alkyl,  $C_{2-8}$  alkenyl,  $C_{2-8}$  alkynyl,  $C_{2-8}$  heteroalkyl,  $C_{2-8}$  aminoalkyl,  $C_{2-8}$  haloalkyl,  $C_{1-8}$  alkoxycarbonyl,  $C_{2-8}$  hydroxyalkyl,  $-C(O)-C_{5-6}$  aryl substituted with  $C_{1-3}$  alkyl or halo,  $C_{5-6}$  aryl,  $C_{5-6}$  heteroaryl,  $C_{5-6}$  cycloalkyl,  $C_{5-6}$  heterocycloalkyl,  $-C(O)NR_{12}R_{13}$ ,  $-CR_5R_{12}R_{13}$ ,  $-(CH_2)_tNR_{12}R_{13}$ ,  $t$  is an integer from 2 to 8; and

each  $R_{12}$  and  $R_{13}$ , independently, is H,  $C_{1-6}$  alkyl;  $C_{3-6}$  cycloalkyl;  $C_{5-6}$  aryl, optionally substituted with halo or  $C_{1-6}$  alkyl; or  $C_{5-6}$  heteroaryl, optionally substituted with halo or  $C_{1-6}$  alkyl; or  $R_{12}$  and  $R_{13}$  together form a cyclic structure; or a pharmaceutically acceptable salt, ester or prodrug thereof.

16. (NEW) The method of claim 1, wherein the compound has the structure of formula (IV):



wherein

$X_1, X_2, X_3, X_4$  and  $X_5$  are selected from C, N and O;

$k$  is 0 or 1;

$t$  is 0, 1 or 2;

$R_1$  is straight or branched-chain  $C_{1-8}$  alkyl,  $C_{2-8}$  alkenyl,  $C_{2-8}$  alkynyl,  $C_{1-8}$  alkylidene,  $C_{1-8}$  alkoxy,  $C_{1-8}$  heteroalkyl,  $C_{1-8}$  aminoalkyl,  $C_{1-8}$  haloalkyl,  $C_{1-8}$  alkoxycarbonyl,  $C_{1-8}$  hydroxyalkoxy,  $C_{1-8}$  hydroxyalkyl,  $-SH$ ,  $C_{1-8}$  alkylthio,  $-O-CH_2-$ ,  $C_{5-6}$  aryl,  $-C(O)-C_{5-6}$  aryl substituted with  $C_{1-3}$  alkyl or halo;  $C_{5-6}$  aryl or  $C_{5-6}$  cycloalkyl optionally comprising 1 or more heteroatoms selected from N, S and O;  $-C(O)NR_3 R_4$ ,  $-NR_3 R_4$ ,  $-NR_3 C(O)NR_4 R_5$ ,  $-CR_3 R_4$ ,  $-OC(O)R_3$ ,  $-(O)(CH_2)_s NR_3 R_4$  or  $-(CH_2)_s NR_3 R_4$ ;

where  $R_3, R_4$  and  $R_5$  are the same or different, each independently being selected from H,  $C_{1-6}$  alkyl;  $C_{5-6}$  aryl optionally comprising 1 or more heteroatoms selected from N, O and S, and optionally substituted with halo or  $C_{1-6}$  alkyl;  $C_{3-6}$  cycloalkyl; or  $R_3$  and  $R_4$  together with the N atom, when present, form a cyclic ring structure comprising 5-6 atoms selected from C, N, S and O; and

$s$  is an integer from 0 to 8;

$A$  is  $C_{5-12}$  aryl or  $C_{5-7}$  cycloalkyl, each optionally comprising 1 or more heteroatoms selected from N, S and O;

$R_2$  is H, amino, hydroxyl, halo, or straight or branched-chain  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  alkoxy,  $C_{1-6}$  heteroalkyl,  $C_{1-6}$  aminoalkyl,  $C_{1-6}$  haloalkyl,  $C_{1-6}$  alkylthio,  $C_{1-6}$  alkoxycarbonyl,  $-CN$ ,  $-CF_3$ ,  $-OR_3$ ,  $-COR_3$ ,  $NO_2$ ,  $-NHR_3$ ,  $-NHC(O)R_3$ ,

--C(O)NR<sub>3</sub> R<sub>4</sub>, --NR<sub>3</sub> R<sub>4</sub>, --NR<sub>3</sub> C(O)NR<sub>4</sub> R<sub>5</sub>, --OC(O)R<sub>3</sub>, --C(O)R<sub>3</sub> R<sub>4</sub>, --O(CH<sub>2</sub>)<sub>q</sub> NR<sub>3</sub>, -  
 -CNR<sub>3</sub> R<sub>4</sub> or --(CH<sub>2</sub>)<sub>q</sub> NR<sub>3</sub> R<sub>4</sub>;

where q is an integer from 1 to 6;

n is 0, 1, 2, 3 or 4, the groups R<sub>2</sub>, when n>1, being the same or different;

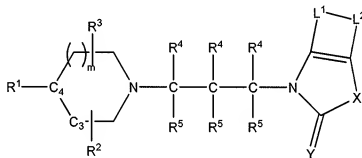
p is 0 or an integer from 1 to 5;

Y is O, S, CHO, --NHC(O)--, --C(O)NH--, --C(O)--, --OC(O)--, NR<sub>7</sub> or --  
 CH=N--, and

R<sub>7</sub> is H or C<sub>1-4</sub> alkyl; or absent; and

Z is CR<sub>8</sub> R<sub>9</sub> wherein R<sub>8</sub> and R<sub>9</sub> are independently selected from H, and straight or  
 branched chain C<sub>1-8</sub> alkyl; or a pharmaceutically acceptable salt, ester or prodrug thereof.

17. (NEW) The method of claim 1, wherein the compound has the structure of  
 formula (V):



(V)

wherein

R<sup>1</sup> is a monoradical selected from the group consisting of optionally substituted  
 C<sub>1-6</sub>-alkyl, optionally substituted C<sub>2-6</sub>-alkylidene, optionally substituted C<sub>2-6</sub>-alkenyl,  
 optionally substituted C<sub>2-6</sub>-alkynyl, optionally substituted O—C<sub>1-6</sub>-alkyl, optionally  
 substituted O—C<sub>2-6</sub>-alkenyl, optionally substituted O—C<sub>2-6</sub>-alkynyl; optionally  
 substituted S—C<sub>1-6</sub>-alkyl, optionally substituted S—C<sub>2-6</sub>-alkenyl, optionally substituted  
 S—C<sub>2-6</sub>-alkynyl;

m is 0, 1 or 2;

C<sub>3</sub>-C<sub>4</sub> is CH<sub>2</sub>—CH or CH=C or C<sub>4</sub> is CH and C<sub>3</sub> is absent;

R<sup>2</sup> and R<sup>3</sup> are independently selected from the group consisting of hydrogen,  
 optionally substituted C<sub>1-6</sub> alkyl, optionally substituted O—C<sub>1-6</sub> alkyl, halogen, hydroxy or  
 selected such that R<sup>2</sup> and R<sup>3</sup> together form a ring system;

each  $R^4$  and  $R^5$  is independently selected from the group consisting of hydrogen, halogen, hydroxy, optionally substituted  $C_{1-6}$ -alkyl, optionally substituted  $O-C_{1-6}$ alkyl, optionally substituted aryl- $C_{1-6}$  alkyl, and optionally substituted arylheteroalkyl;

$L^1$  and  $L^2$  are biradicals independently selected from the group consisting of  $-C(R^6)=C(R^7)-$ ,  $-C(R^6)=N-$ ,  $-N=C(R^6)-$ ,  $-S-$ ,  $-NH-$  and  $-O-$ ; wherein only one of  $L^1$  and  $L^2$  may be selected from the group consisting of  $-S-$ ,  $-NH-$  and  $-O-$ ;

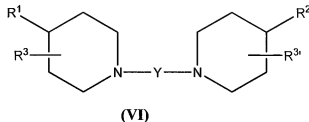
Y is selected from the group consisting of O, S, and  $H_2$ ;

X is a biradical selected from the group consisting of  $-C(R^6)(R^7)-C(R^6)(R^7)-$ ,  $-C(R^6)=C(R^7)-$ ,  $-O-C(R^6)(R^7)-$ ,  $C(R^6)(R^7)-O-$ ,  $-S-C(R^6)(R^7)-$ ,  $-C(R^6)(R^7)-S-$ ,  $-N(R^N)-C(R^6)(R^7)-$ ,  $-C(R^6)(R^7)-N(R^N)-$ ,  $-C(R^6)(R^7)-C(R^6)(R^7)-$ ,  $-O-C(R^6)(R^7)-C(R^6)(R^7)-$ ,  $S-C(R^6)(R^7)-C(R^6)(R^7)-$ ,  $N(R^N)-C(R^6)(R^7)-C(R^6)(R^7)-$ ,  $-C(R^6)(R^7)-C(R^6)(R^7)-O-$ ,  $-C(R^6)(R^7)-C(R^6)(R^7)-S-$ ,  $-C(R^6)(R^7)-C(R^6)(R^7)-N(R^N)-$ ,  $-C(R^6)(R^7)-C(R^6)=C(R^7)-$ , and  $-C(R^6)=C(R^7)-C(R^6)(R^7)-$ ,

wherein  $R^6$  and  $R^7$  are independently selected from the group consisting of hydrogen, halogen, hydroxy, nitro, cyano,  $NR^N R^N$ ,  $N(R^N)-C(O)N(R^N)$ , optionally substituted  $C_{1-6}$ -alkyl,  $C_{2-6}$ -alkenyl,  $C_{2-6}$ -alkynyl, , optionally substituted  $O-C_{1-6}$ -alkyl, optionally substituted  $O$ -aryl, optionally substituted  $O-C_{2-6}$ -alkenyl, optionally substituted  $O-C_{2-6}$ -alkynyl, and

wherein  $R^N$  is selected from the group consisting of hydrogen, and optionally substituted  $C_{1-6}$ -alkyl.

18. (NEW) The method of claim 1, wherein the compound has the structure of formula (VI):



wherein

Y is a biradical of  $(CR^4R^5)_m-Z-C(R^4R^5)_n$ ;



wherein the sum  $m+n$  is from 1 to 7;

Z is selected from the group consisting of  $C(R^4R^5)$ ,  $C(O)$ ,  $O$ ,  $N(R^6)$ ,  $S$ ,  $O-C(O)$ ,  $N(R^6)C(O)$ ,  $C(O)-O$ , and  $P$ ; and

$R^4$  and  $R^5$  are independently selected from the group consisting of hydrogen, halogen, hydroxy, nitro,  $NR^6N^{6'}$ , optionally substituted aryl, optionally substituted heteroaryl, optionally substituted  $C_{3-8}$ -cycloalkyl, optionally substituted heterocyclyl, optionally substituted  $C_{1-6}$ -alkyl, optionally substituted  $C_{1-6}$ -alkoxy, optionally substituted phenoxy, optionally substituted  $C_{2-8}$ -alkenyl and optionally substituted  $C_{2-8}$ -alkynyl; and

wherein  $R^1$  and  $R^2$  are independently selected from the group consisting of optionally substituted aryl, optionally substituted heteroaryl, optionally substituted  $C_{3-8}$ -cycloalkyl, optionally substituted heterocyclyl, optionally substituted  $C_{1-6}$ -alkyl, optionally substituted  $C_{1-6}$ -alkoxy, optionally substituted  $C_{2-8}$ -alkenyl and optionally substituted  $C_{2-8}$ -alkynyl;

wherein  $R^3$  and  $R^{3'}$  are independently selected from the group consisting of hydrogen, halogen, hydroxy, nitro,  $NR^6N^{6'}$ , optionally substituted aryl, optionally substituted heteroaryl, optionally substituted  $C_{3-8}$ -cycloalkyl, optionally substituted heterocyclyl, optionally substituted  $C_{1-6}$ -alkyl, optionally substituted  $C_{1-6}$ -alkoxy, optionally substituted  $C_{2-8}$ -alkenyl and optionally substituted  $C_{2-8}$ -alkynyl; and

$R^6$  and  $R^{6'}$  are independently selected from the group consisting of hydrogen, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted  $C_{3-8}$ -cycloalkyl, optionally substituted heterocyclyl, optionally substituted  $C_{1-6}$ -alkyl, optionally substituted  $C_{1-6}$ -alkoxy, optionally substituted  $C_{2-8}$ -alkenyl and optionally substituted  $C_{2-8}$ -alkynyl.